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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/085,820	05/28/1998	HAI U. WANG	CIT98-01PA	7434

21005 7590 04/29/2002

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EXAMINER

ANDRES, JANET L

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 04/29/2002

24

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/085,820

**Applicant(s)**

WANG ET AL.

**Examiner**

Janet L Andres

**Art Unit**

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 25 March 2002.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 3-6, 10, 11, 42, 72, 74, 76-79, 82 and 84-152 is/are pending in the application.
- 4a) Of the above claim(s), See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3, 5, 10, 42, 72, 74, 76, 77, 79, 82, 85, 89-91, 93, 94, 98-102, 116, 121-126 and 129-132 is/are rejected.
- 7) ☒ Claim(s) 133, 134, 136-138, 143-146, 148, 149, 151, 152 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

Continuation of Disposition of Claims: Claims withdrawn from consideration are 4,6,11,78,84,86-88,92,95-97,103-115,117-120,127,128,135,139-142,147 and 150.

### **RESPONSE TO AMENDMENT**

1. Applicant's amendment filed 25 March 2002 is acknowledged. Claims 3-6, 10, 11, 42, 72, 74, 76-79, 82, and 84-152 are pending in this application. Claims 4, 6, 11, 78, 84, and new claims 86-88, 92, 95-97, 103-115, 117-120, 127, 128, 135, 139-142, 147, and 150 are withdrawn from consideration as drawn to a non-elected invention. Claims 3, 5, 10, 42, 72, 74, 76, 77, 79, 82, 85, 89-91, 93, 94, 98-102, 116, 121-126, 129-134, 136-138, 143-146, 148, 149, 151 and 152 encompass the elected invention, *in vivo* methods of altering angiogenesis using an angiogenic factor that affects artery-specific molecules, and are under consideration in this office action. The examiner notes that, as claimed, an "ephrin B2 agonist" would interact with veins while an "ephB4 agonist" would interact with arteries. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

#### ***Claim Rejections Withdrawn***

2. The provisional double patenting rejection is withdrawn in response to Applicant's cancellation of the relevant claims in 09/687652.

#### ***Claim Rejections Maintained***

3. The rejection of claims 3, 5, 42, 76, 77, and 85 under 35 U.S.C. 112, first paragraph, as lacking enablement commensurate with the scope of the claims is maintained, newly applied to claim 74, and applied to new claims 89-91, 93, 94, 98-102, 116, 121-126, and 129-132.

The original basis of this rejection was that, while one of skill in the art could identify ephrin/eph pairs in arteries and veins, one of skill in the art could not predict that they would be involved in angiogenesis.

Applicant's disclosure and the teachings of Adams et al. indicate that some ephrin B ligands and ephB receptors are involved in the development of the vascular system. Applicant argues that methods of disclosing tissue localization have been disclosed, and that the structural characteristics of ephrin ligands and eph receptors are presented. Applicant argues that differentially expressed genes could be readily identified. Applicant points to the teachings of Adams et al. as demonstrating that ephB2 and ephB3 are also involved in angiogenesis. Applicant further argues that Applicant's teachings are a pioneering invention that provides motivation for others to examine other ephrin ligands and eph receptors.

Applicant's arguments are sufficient to overcome the original basis of the rejection, that one of skill could not predictably find other eph receptors and ephrin ligands that are involved in angiogenesis. The teachings of Adams et al. indicate that other eph receptors are involved in angiogenesis. One of skill in the art could thus expect to identify other eph receptors and ephrin ligands, and, based on the teachings of Adams et al., would expect to find that some such molecules were involved in angiogenesis.

However, one of skill in the art would still not be able to use the invention as broadly claimed. What is required for Applicant's invention is that enhancing the interaction between an eph receptor and an ephrin ligand result in angiogenesis, and that addition of a soluble eph receptor result in angiogenesis. Applicant has not, however, taught how the interaction of a receptor and ligand might be enhanced. What is described in the specification is a way of screening for enhancers. No enhancing molecules are described, and there are no teachings to indicate that such molecules exist and what their characteristics would be. Further, there is no direction in Applicant's disclosure that would indicate to one of skill in the art that enhancement

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of this interaction would alter angiogenesis. What is provided is thus the idea for an invention, and the invitation to experiment to implement this invention, not the invention itself.

Furthermore, Applicant has provided no guidance to indicate that a soluble receptor would enhance, rather than inhibit, angiogenesis. Such a soluble receptor would block cell-cell interactions, and the results of such a block are not readily predictable. If other cellular interactions are required for angiogenesis, a soluble receptor would be inhibitory. There are no teachings in the specification that would allow one of skill in the art to predict the outcome of using such a receptor.

The teachings of Adams et al. serve to further indicate that the interactions between ephs and ephrins are complex and the outcome of affecting such interactions is unpredictable (pages 301-302). Adams et al. indicate that receptors and ligands are both found on veins, and that the interactions between ligands and receptors are promiscuous. Adams et al. conclude that “the mechanism of ephrin B and Eph receptor function *in vivo* is unclear” (p. 302).

Thus, while one of skill in the art might be able to identify other eph receptors and ephrin ligands involved in angiogenesis, one of skill in the art would not be able predictably enhance this interaction; Applicant has not provided sufficient guidance as to what type of agent could be used for this purpose. One of skill in the art could further not predict the results of enhancing this interaction, or of the use of a soluble receptor. Applicant provides no teachings to indicate that these methods increase angiogenesis, and the teachings of Adams et al. further indicate that the interactions involved, and the results of these interactions, are not fully understood. Thus, it would require undue experimentation for the skilled artisan to make and use the invention as claimed.

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4. Claims 10, 72, 79, and 82 are newly rejected under 35 U.S.C. 112, second paragraph, because they do not require that the ligand be expressed on arterial cells. Since ephrins are expressed elsewhere, such a limitation is required for the skilled artisan to be able to determine what ligands were intended.

5. Claims 3, 10, 42, 74, 76, 77, 85, 94, 116, 125, 126, 129, 130-134, 136-138, 143-149, 151, and 152 are objected to because they encompass non-elected inventions or depend from claims that do.

CLAIMS 3, 5, 10, 42, 72, 74, 76, 77, 79, 82, 85, 89, 90, 91, 93, 94, 98-102, 116, 121-126, AND 129-132 ARE REJECTED. CLAIMS 133, 134, 136-138, 143-146, 148, 149, 151, AND 152 ARE OBJECTED TO.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 872-9306 or (703) 872-9307 for after final communications.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].


All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that

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sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.  
April 24, 2002



**LORRAINE SPECTOR  
PRIMARY EXAMINER**